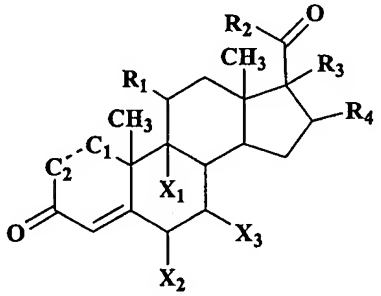
AMENDMENTS TO THE CLAIMS

Kindly amend claim 12 and cancel claims 13, 26, and 27 as provided in the following Claims Listing.

Claims Listing:

Claims 1-11 (cancelled).

12. (currently amended) A method of treating for therapeutic purposes a mammal suffering from an autoimmune or inflammatory condition, said method comprising administering to said mammal a corticosteroid conjugate comprising a corticosteroid attached via a linker to ~~a group that is either~~ a bulky group of greater than 400 daltons ~~or a charged group of less than 400 daltons~~ in an amount effective to treat said condition, said corticosteroid conjugate (i) having anti-inflammatory activity *in vivo*, (ii) having reduced activity in the central nervous system in comparison to said corticosteroid without said group, and (iii) being resistant to *in vivo* cleavage, such that *in vivo* less than 10% of the administered corticosteroid conjugate is cleaved, separating said corticosteroid from said group, prior to excretion~~.~~, wherein said corticosteroid is described by formula I:



I

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

X_2 represents -H, $-CH_3$, or a halogen atom;

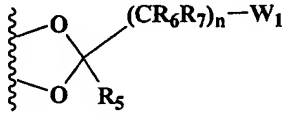
X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents $-CH_3$, $-SCH_2F$, $-CH_2Cl$, $-CH_2$-G, $-CH_2OH$, $-CH_2O$-$P(O)(O^-)_2$, CH_2O-acyl, $-CH_2NH$-G^1, $-CH_2S$-G^1, or $-CH_2O$-G^1;

R_3 and R_4 each, independently, represents -H, $C_{1\text{-}10}$ alkyl, -OH, -O-acyl, -O-G^1, or

R_3 and R_4 combine to form a cyclic acetal of formula II wherein:



II

n is an integer from 0 to 6;

R_5, R_6, and R_7 each, independently, represents -H or $C_{1\text{-}10}$ alkyl;

W_1 represents -H, $-CH_3$, -G^1, $-NR_8$-G^1, –NH-NH-G^1, ~~-O-G^1;~~ -S-G^1, or -C(O)-G^1, ~~or -C(S)-G^1~~;

R_8 represents -H, $C_{1\text{-}10}$ alkyl or $C_{5\text{-}10}$ aryl; and

G^1 is a bond between said corticosteroid and said linker;

and wherein said linker is described by formula III:

$$G^1\text{-}(Z^1)_o\text{-}(Y^1)_u\text{-}(Z^2)_s\text{-}(R_{10})\text{-}(Z^3)_t\text{-}(Y^2)_v\text{-}(Z^4)_p\text{–}G^2 \qquad \text{III}$$

wherein

G^1 is a bond between said corticosteroid and said linker;

G^2 is a bond between said linker and said bulky group ~~or between said linker and said charged group~~;

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from ~~O,~~ S, and NR_{11};

R_{11} is hydrogen or a $C_{1\text{-}10}$ alkyl group;

Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1; ~~and~~

R_{10} is a $C_{1\text{-}10}$ alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched $C_{2\text{-}10}$ alkene, a linear or branched $C_{2\text{-}10}$ alkyne, a $C_{5\text{-}10}$ aryl, a cyclic system of 3 to 10 atoms, $-(CH_2CH_2O)_qCH_2CH_2-$ in which q is an integer of 1 to 4, or a chemical bond linking $G^1-(Z^1)_o-(Y^1)_u-(Z^2)_s-$ to $-(Z^3)_t-(Y^2)_v-(Z^4)_p-G^2$; and

(a) said corticosteroid and said linker are connected via a first linkage group, and (b) said linker and said bulky group are connected via a second linkage group, each of said first linkage group and said second linkage group selected, independently, from an amine, amide, hydrazide, or thioether linkage;

and wherein said condition is selected from asthma, psoriasis, eczema, organ/tissue transplant rejection, graft vs. host reactions, Raynaud's syndrome, autoimmune thyroiditis, Grave's disease, autoimmune hemolytic anemia, autoimmune thromboeytopenia purpura, mixed connective tissue disease, idiopathic Addison's disease, Sjogren's syndrome, urticaria, dermatitis, multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, uveitis, Crohn's disease, ulcerative colitis, lupus, tendonitis, bursitis, adult respiratory distress syndrome, shock, oxygen toxicity, glomerulonephritis, vasculitis, reactive arthritis, necrotizing enterocolitis, Goodpasture's syndrome, hypersensitivity pneumonitis, glomerulonephritis; encephalomyelitis, and meningitis.

13. (cancelled).

14. (original) The method of claim 12, wherein said condition is rheumatoid arthritis or colitis.

15. (original) The method of claim 12, wherein said corticosteroid conjugate is administered by intravenous, intraperitoneal, subcutaneous, ocular, topical, nasal, or intramuscular administration.

Claims 16-21 (cancelled).

22. (previously presented) The method of claim 12, wherein said corticosteroid conjugate comprises a corticosteroid attached to a bulky group and said bulky group comprises a naturally occurring polymer or a synthetic polymer.

23. (previously presented) The method of claim 22, wherein said bulky group comprises a glycoprotein, a polypeptide, or a polysaccharide.

24. (withdrawn) The method of claim 22, wherein said bulky group comprises hyaluronic acid or alpha-1-acid glycoprotein.

25. (previously presented) The method of claim 22, wherein said bulky group comprises polyethylene glycol or N-hxg.

26. (cancelled).

27. (cancelled).

28. (previously presented) The method of claim 12, wherein said corticosteroid conjugate comprises a corticosteroid attached to a bulky group and said bulky group comprises a corticosteroid.

29. (previously presented) The method of claim 12, wherein said corticosteroid conjugate comprises a corticosteroid attached to a bulky group of greater than 600 daltons.

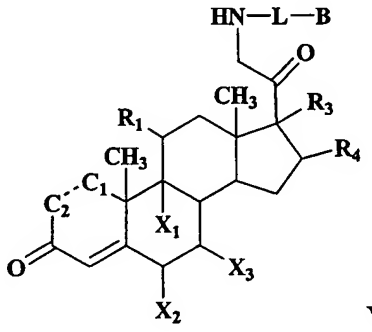
30. (previously presented) The method of claim 12, wherein said corticosteroid conjugate comprises a corticosteroid attached to a bulky group of greater than 800 daltons.

31. (previously presented) The method of claim 12, wherein said corticosteroid conjugate is resistant to *in vivo* cleavage, such that *in vivo* less than 5% of the administered corticosteroid conjugate is cleaved, separating said corticosteroid from said group, prior to excretion.

32. (previously presented) The method of claim 12, wherein said corticosteroid conjugate is resistant to *in vivo* cleavage, such that *in vivo* less than 2% of the administered corticosteroid conjugate is cleaved, separating said corticosteroid from said group, prior to excretion.

33. (previously presented) The method of claim 12, wherein said corticosteroid is selected from beclomethasone, budesonide, prednisolone, prednisone, and triamcinolone.

34. (withdrawn) The method of claim 12, wherein said corticosteroid conjugate is described by formula V:



V

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

X_2 represents -H, $-CH_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_3 and R_4 each, independently, represents -H, $C_{1\text{-}10}$ alkyl, -OH, or -O-acyl,

L is a linker described by formula III:

$$-(Z^1)_o-(Y^1)_u-(Z^2)_s-(R_{10})-(Z^3)_t-(Y^2)_v-(Z^4)_p- \quad \text{III}$$

wherein

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR_{11};

R_{11} is hydrogen or a $C_{1\text{-}10}$ alkyl group;

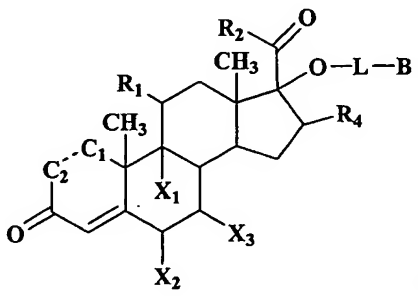
Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1;

R_{10} is a $C_{1\text{-}10}$ alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched $C_{2\text{-}10}$ alkene, a linear or branched $C_{2\text{-}10}$ alkyne, a $C_{5\text{-}10}$ aryl, a cyclic system of 3 to 10 atoms, $-(CH_2CH_2O)_qCH_2CH_2-$ in which q is an integer of 1 to 4, or a chemical bond linking $-(Z^1)_o-(Y^1)_u-(Z^2)_s-$ to $-(Z^3)_t-(Y^2)_v-(Z^4)_p-$; and

B is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons.

35. (withdrawn) The method of claim 12, wherein said corticosteroid conjugate is described by formula VI:



VI

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

X_2 represents -H, $-CH_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents $-CH_3$, $-SCH_2F$, $-CH_2Cl$, $-CH_2OH$, $-CH_2O-P(O)(O^-)_2$, or CH_2O-acyl;

R_4 represents -H, C_{1-10} alkyl, -OH, or -O-acyl;

L is a linker described by formula III:

$$-(Z^1)_o-(Y^1)_u-(Z^2)_s-(R_{10})-(Z^3)_t-(Y^2)_v-(Z^4)_p- \quad \text{III}$$

wherein

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR_{11};

R_{11} is hydrogen or a C_{1-10} alkyl group;

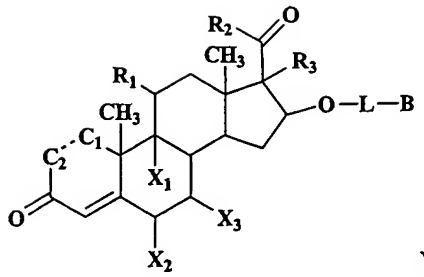
Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1;

R_{10} is a C_{1-10} alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched C_{2-10} alkene, a linear or branched C_{2-10} alkyne, a C_{5-10} aryl, a cyclic system of 3 to 10 atoms, $-(CH_2CH_2O)_qCH_2CH_2-$ in which q is an integer of 1 to 4, or a chemical bond linking $-(Z^1)_o-(Y^1)_u-(Z^2)_s-$ to $-(Z^3)_t-(Y^2)_v-(Z^4)_p-$; and

B is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons.

36. (withdrawn) The method of claim 12, wherein said corticosteroid conjugate is described by formula VII:



VII

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

X_2 represents -H, $-CH_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents $-CH_3$, $-SCH_2F$, $-CH_2Cl$, $-CH_2OH$, $-CH_2O-P(O)(O^-)_2$, or CH_2O-acyl;

R_3 represents -H, C_{1-10} alkyl, -OH, or -O-acyl;

L is a linker described by formula III:

$$-(Z^1)_o-(Y^1)_u-(Z^2)_s-(R_{10})-(Z^3)_t-(Y^2)_v-(Z^4)_p- \quad \text{III}$$

wherein

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR_{11};

R_{11} is hydrogen or a C_{1-10} alkyl group;

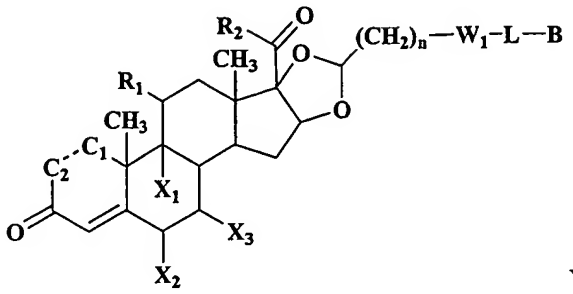
Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1;

R_{10} is a C_{1-10} alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched C_{2-10} alkene, a linear or branched C_{2-10} alkyne, a C_{5-10} aryl, a cyclic system of 3 to 10 atoms, $-(CH_2CH_2O)_qCH_2CH_2-$ in which q is an integer of 1 to 4, or a chemical bond linking $-(Z^1)_o-(Y^1)_u-(Z^2)_s-$ to $-(Z^3)_t-(Y^2)_v-(Z^4)_p-$; and

B is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons.

37. (withdrawn) The method of claim 12, wherein said corticosteroid conjugate is described by formula VIII:



VIII

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

X_2 represents -H, $-CH_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents $-CH_3$, $-SCH_2F$, $-CH_2Cl$, $-CH_2OH$, $-CH_2O-P(O)(O^-)_2$, or CH_2O-acyl;

n is an integer from 0 to 6;

W_1 represents $-NR_8-$, –NH-NH-, -O-, -S-, -C(O)-, or -C(S)-;

R_8 represents -H, C_{1-10} alkyl or C_{5-10} aryl;

L is a linker described by formula III:

$$-(Z^1)_o-(Y^1)_u-(Z^2)_s-(R_{10})-(Z^3)_t-(Y^2)_v-(Z^4)_p- \quad \text{III}$$

wherein

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR_{11};

R_{11} is hydrogen or a C_{1-10} alkyl group;

Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1;

R_{10} is a C_{1-10} alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or

branched $C_{2\text{-}10}$ alkene, a linear or branched $C_{2\text{-}10}$ alkyne, a $C_{5\text{-}10}$ aryl, a cyclic system of 3 to 10 atoms, $-(CH_2CH_2O)_qCH_2CH_2-$ in which q is an integer of 1 to 4, or a chemical bond linking $-(Z^1)_o-(Y^1)_u-(Z^2)_s-$ to $-(Z^3)_t-(Y^2)_v-(Z^4)_p-$; and

B is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons.